

AMENDMENTS TO THE CLAIMS

1-27. (canceled)

28. (currently amended) A ~~WRAP-PROBE~~ method for detecting a target nucleotide sequence, and providing a partial helical enclosure of the target sequence, comprising the steps of:

a) rendering the target nucleotide sequence substantially single-stranded ~~to give a single-stranded target nucleotide sequence;~~

b) hybridizing the single-stranded target nucleotide sequence with a nucleic acid probe unit ~~, thereby forming a hybridized WRAP-PROBE complex of a single-stranded target nucleotide sequence and a nucleic acid probe, said WRAP-PROBE comprising (i) a central sequence complementary to the single-stranded target nucleotide sequence[[s]], and (ii) further comprising a probe linker at each of the two one or both terminal ends of the probe unit, said probe linker comprises comprising a single-stranded nucleotide sequence that hybridizes to a reporter linker of a reporter but does not hybridize to the single-stranded target nucleotide sequence, wherein said probe linker sequence is joined to one or more reporters, either prior to or subsequent to the hybridization of the probe to the target sequence;~~

c) washing to remove any unbound probe;

d) hybridizing reporters joining said reporter to the two said probe linkers ~~linker, if not previously joined; and~~

e) detecting the presence of the reporter ~~said reporter or reporters~~ to indicate the presence of the target nucleotide sequence.

29. (currently amended) The method of claim 28, wherein the probe unit comprises a first oligonucleotide comprising a sequence complementary to the single-stranded target nucleotide sequence flanked by a first probe linker on one end and an overlap linker on the other end, said overlap linker is hybridized to a second oligonucleotide comprising a second probe linker ~~comprises a first terminal probe linker.~~

30. (currently amended) The method of claim 28, wherein the reporter comprises a labeled, double-stranded polynucleotide sequence linked on one or both ends to a reporter linker that comprises a short single-stranded polynucleotide ~~probe comprises a first terminal probe linker and a second terminal probe linker.~~

31. (currently amended) The method of claim 30, wherein the ~~reporter is a labeled, double-stranded polynucleotide sequence is at least 100 bases long and the short single-stranded polynucleotide linker is from about 20 bases to about 30 bases long, known as a GENE TAG, having one or more said first reporter linkers, said first reporter linker comprising a single stranded nucleotide sequence hybridized to the first terminal probe linker.~~

32. (currently amended) The method of claim 30, wherein two ~~one or more~~ reporters form ~~comprise~~ a reporter array by linking end-to-end via the reporter linker ~~, said array comprising a first labeled, double stranded polynucleotide sequence, known as a GENE TAG, linked together end to end by hybridization to one or more GENE TAGS, wherein said first GENE TAG comprises one or more first reporter linkers, said first reporter linker comprising a single stranded nucleotide sequence hybridizable to said first terminal probe linker, and one or more second reporter linkers hybridized to one or more first reporter linkers of a second GENE TAG, and wherein said second GENE TAG further comprises one or more second reporter linkers, and optionally, additional GENE TAGs linked to the remainder of the array by hybridization of the first reporter linker of each subsequent GENE TAG to the second reporter linker of the preceding GENE TAG in the array, to form a chained or branch configuration having one or more ends, wherein said terminal end comprises the second reporter linker of a terminal GENE TAG.~~

33. (currently amended) The method of claim 32, wherein the length of the reporter array is determined by a ratio of terminator oligonucleotide to reporters, said terminator oligonucleotide terminates the reporter array by hybridizing to a reporter linker at the end of the reporter array further comprising one or more terminators, said terminator comprising a

~~single stranded polynucleotide sequence complementary to said second reporter linker of one or more terminal GENE TAGs, such that said terminator forms said terminal end.~~

34. (currently amended) The method of claim 28, ~~wherein the reporter is joined directly to the first terminal probe linker.~~ 32, wherein the reporter array comprises successive layers of type I and type II reporters, each of the type I and type II reporter comprises a first and a second reporter linker, wherein the first and second reporter linker of a type I reporter is hybridized respectively to the second reporter linker of a type II reporter and to the first reporter linker of another type II reporter, except the first reporter linker of the type I reporter in the first layer of reporter is hybridized to a probe linker of a probe.

35. (currently amended) The method of claim 28, ~~wherein the reporter is joined indirectly to the first terminal probe linker, further comprising a multi-linking unit is interposed between said the reporter and the terminal probe linker, said multi-linking unit comprises (i) a sequence that hybridizes to the probe linker and (ii) two or more sequences that hybridize to the reporter linker of the reporter unit known as a Multi-LINKER, comprising a first polynucleotide comprising a first terminal unit linker, a second terminal unit linker, and at least one internal linker, wherein said first terminal unit linker is hybridized to said first terminal probe linker, and wherein at least two of said internal and second terminal unit linkers are hybridized to one or more reporters, and wherein said first and second terminal unit linkers and said internal linker are not hybridizable to a target sequence of said probe.~~

36-37. (canceled)

38. (currently amended) A ~~WRAP-LOCK~~ method for detecting a target nucleotide sequence and providing a circular enclosure of the target sequence polynucleotide strand with a WRAP-PROBE, comprising the steps of:

a) providing a first probe comprising (i) sequence complementary to a first region of the target sequence and (ii) non-target sequence that does not hybridize to the target sequence ~~the WRAP-PROBE of Claim 30;~~

b) providing a second probe comprising (i) sequence complementary to a second region of the target sequence and (ii) non-target sequence that does not hybridize to the target sequence ~~a RING-LOCK Unit comprising at least two single-stranded polynucleotides, wherein at least one single-stranded polynucleotide is joined or suitable for joining to said first terminal probe linker, and wherein at least one single-stranded polynucleotide is joined or suitable for joining to one or more reporters;~~

c) providing a first ring subunit comprising (i) sequence complementary to the non-target sequence of the first probe, (ii) reporter linker that hybridizes to reporter sequence, and (iii) a overlapping region complementary to a region of a second ring subunit ~~treating the probe and RING-TAIL unit, at this step or another step, to effect cross-linking or to increase binding;~~

d) providing a second ring subunit comprising (i) sequence that hybridizes to a reversing oligonucleotide, (ii) reporter linker that hybridizes to reporter sequence, and (iii) a overlapping region complementary to the overlapping region of the first ring subunit, wherein the reversing oligonucleotide comprises sequence that hybridizes to the non-target sequence of the second probe and sequence that hybridizes to the second ring subunit ~~hybridizing the WRAP-PROBE to the target strand, thereby forming a hybridized complex;~~

e) forming a circular enclosure to the target sequence by hybridizing the first and second probes to the target sequence, wherein the first probe is hybridized to the first ring subunit, and the second probe is hybridized to the reversing oligonucleotide which is hybridized to the second ring subunit, wherein the first and second ring subunits are hybridized to each other at the overlapping region ~~joining at least one single-stranded polynucleotide to said first terminal probe linker, if not previously joined;~~

f) joining the first and second probes by ligation ~~providing a looping nucleotide comprising a first region complementary to said second terminal probe linker, and a second region complementary to said RING-TAIL Unit, wherein said looping nucleotide~~

~~hybridizes to the second terminal probe linker and the RING-TAIL Unit, thereby forming a closed loop about the target strand;~~

g) hybridizing reporter sequences to the reporter linkers of the first and second ring subunits ~~joining a reporter or reporters to at least one ring tail linker, if not previously attached, or if more or needed; and~~

h) detecting the presence of reporter sequences to indicate the presence of target sequence.

39. (currently amended) A ~~DOUBLE WRAP LOCK~~ method of simultaneously detecting a target sequence on both a sense and anti-sense strand of DNA, comprising the steps of:

a) providing a first probe comprising (i) sequence complementary to a first region of the target sequence on the sense strand DNA, and (ii) non-target sequence that does not hybridize to the target sequence ~~a double-stranded DNA comprising an antisense strand and a sense strand, wherein both said antisense strand and said sense strand comprise a target sequence;~~

b) providing a second probe comprising (i) sequence complementary to a second region of the target sequence on the sense strand DNA, and (ii) non-target sequence that does not hybridize to the target sequence ~~sense WRAP PROBE of Claim 30, said sense WRAP PROBE probe having a central sequence complementary to the sense-strand target sequence;~~

c) providing a first ring subunit comprising (i) sequence complementary to the non-target sequence of the first probe, (ii) reporter linker that hybridizes to reporter sequence, and (iii) a overlapping region complementary to a region of a second ring subunit ~~an antisense WRAP PROBE probe of Claim 30, said antisense WRAP LOCK probe having a central sequence complementary to the antisense strand target sequence;~~

d) providing a second ring subunit comprising (i) sequence that hybridizes to a reversing oligonucleotide, (ii) reporter linker that hybridizes to reporter sequence, and (iii) a overlapping region complementary to the overlapping region of the first ring subunit, wherein the reversing oligonucleotide comprises sequence that hybridizes to the non-target

~~sequence of the second probe and sequence that hybridizes to the second ring subunit first RING TAIL Unit comprising at least two first single stranded polynucleotides, wherein at least one first single stranded polynucleotide is joined or suitable for joining to said first terminal probe linker of said sense WRAP PROBE, and wherein at least one first single stranded polynucleotide is joined or suitable for joining to one or more first reporters;~~

~~e) providing a third probe comprising (i) sequence complementary to a first region of the target sequence on the anti-sense strand DNA, and (ii) non-target sequence that does not hybridize to the target sequence providing a second RING LOCK Unit comprising at least two second single stranded polynucleotides, wherein at least one second single stranded polynucleotide is joined or suitable for joining to said first terminal probe linker of said antisense WRAP PROBE, and wherein at least one second single stranded polynucleotide is joined or suitable for joining to one or more second reporters, wherein said second reporter produces a signal distinct from said first reporter;~~

~~f) providing a fourth probe comprising (i) sequence complementary to a second region of the target sequence on the anti-sense strand DNA, and (ii) non-target sequence that does not hybridize to the target sequence treating the WRAP PROBES and the RING LOCK Units, at this step or another step, to effect cross-linking or to increase binding;~~

~~g) providing a third ring subunit comprising (i) sequence complementary to the non-target sequence of the third probe, (ii) reporter linker that hybridizes to reporter sequence, and (iii) a overlapping region complementary to a region of a fourth ring subunit hybridizing said sense WRAP PROBE to the sense strand, thereby forming a sense hybridized complex; and hybridizing said antisense WRAP PROBE to the antisense strand, thereby forming an antisense hybridized complex;~~

~~h) providing a fourth ring subunit comprising (i) sequence that hybridizes to a reversing oligonucleotide, (ii) reporter linker that hybridizes to reporter sequence, and (iii) a overlapping region complementary to the overlapping region of the third ring subunit, wherein the reversing oligonucleotide comprises sequence that hybridizes to the non-target sequence of the fourth probe and sequence that hybridizes to the fourth ring subunit joining at least one first single stranded polynucleotide to said first terminal probe linker of said~~

~~sense WRAP PROBE, if not so previously joined; and joining at least one second single-stranded polynucleotide to said first terminal probe linker of said antisense WRAP PROBE, if not so previously joined;~~

~~i) forming a first circular enclosure to the target sequence on the sense strand DNA by hybridizing the first and second probes to the target sequence on the sense strand DNA, wherein the first probe is hybridized to the first ring subunit, and the second probe is hybridized to the reversing oligonucleotide which is hybridized to the second ring subunit, wherein the first and second ring subunits are hybridized to each other at the overlapping region providing a first looping nucleotide comprising a first region complementary to said second terminal probe linker of said sense WRAP PROBE, and a second region complementary to said first RING TAIL Unit, wherein said looping nucleotide hybridizes and thereby forms a closed loop about the target sense strand; and providing a second looping nucleotide comprising a first region complementary to said second terminal probe linker of said antisense WRAP PROBE, and a second region complementary to said second RING TAIL Unit, wherein said looping nucleotide hybridizes and thereby forms a closed loop about the target antisense strand;~~

~~j) forming a second circular enclosure to the target sequence on the anti-sense strand DNA by hybridizing the third and fourth probes to the target sequence on the anti-sense strand DNA, wherein the third probe is hybridized to the third ring subunit, and the fourth probe is hybridized to the reversing oligonucleotide which is hybridized to the fourth ring subunit, wherein the third and fourth ring subunits are hybridized to each other at the overlapping region joining one or more first reporters to at least one said first single-stranded polynucleotide, if not so previously joined; joining one or more second reporters to at least one said second single-stranded polynucleotide, if not previously joined, wherein said second reporter produces a signal distinct from said first reporter;~~

~~k) determining whether the sense target sequence is present by detecting the presence or absence of said first reporter or reporters; or determining whether the antisense target sequence is present by detecting the presence or absence of said second reporter or reporters, or both. joining the first and second probes by ligation;~~

~~l) joining the third and fourth probes by ligation;~~

m) hybridizing reporter sequences to the reporter linkers of the first and second ring subunits, thereby forming a first reporter signal;

n) hybridizing reporter sequences to the reporter linkers of the third and fourth ring subunits, thereby forming a second reporter signal; and

o) detecting the presence of reporter sequences to indicate the presence of target sequences on the sense and anti-sense strand DNA.

40-57. (canceled)

58. (new) A method of detecting a target nucleotide sequence and providing a circular enclosure of the target sequence, comprising the steps of:

a) providing a probe comprising (i) sequence complementary to the target sequence, (ii) sequence that hybridizes to a first ring subunit, and (iii) sequence that hybridizes to a lock oligonucleotide, wherein the lock oligonucleotide comprises sequence that hybridizes to the probe and sequence that hybridizes to a second ring subunit;

b) providing a first ring subunit comprising (i) sequence that hybridizes to the probe, (ii) reporter linker that hybridizes to reporter sequence, and (iii) a overlapping region complementary to a region of the second ring subunit;

d) providing the second ring subunit comprising (i) sequence that hybridizes to the lock oligonucleotide, (ii) reporter linker that hybridizes to reporter sequence, and (iii) a overlapping region complementary to the overlapping region of the first ring subunit;

e) forming a circular enclosure to the target sequence by hybridizing the probe to the target sequence, wherein the probe is hybridized to the first ring subunit which is hybridized to the second ring subunit at the overlapping region, and the lock oligonucleotide is hybridized to the second ring subunit and the probe;

f) hybridizing reporter sequences to the reporter linkers of the first and second ring subunits; and

g) detecting the presence of reporter sequences to indicate the presence of target sequence.

59. (new) The method of claim 29, wherein the overlap linker comprises one or more TA sequence to facilitate crosslinking during probe fabrication.

60. (new) The method of claim 30, wherein the reporter linker comprises a carbon spacer segment.

61. (new) The method of claim 30, wherein the reporter linker comprises sequence selected from the group consisting of SEQ ID NO. 6, 10, 71, 76 and 81.